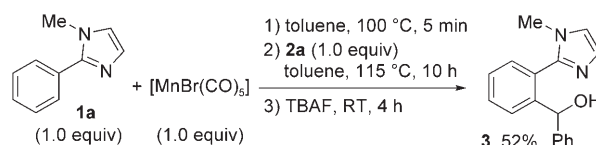


Manganese-Catalyzed Insertion of Aldehydes into a C–H Bond**

Yoichiro Kuninobu,* Yuta Nishina, Takahiro Takeuchi, and Kazuhiko Takai*

Transition metals of the fourth row are abundant and cheap compared to those of the fifth and sixth rows. Therefore, by introducing new reactivities with fourth-row metal complexes, it might be possible to replace fifth- and sixth-row metals in some fundamental and important reactions. Catalytic Grignard-type addition of nucleophiles to aldehydes is one such reaction. Grignard reagents are usually prepared from organic halides and magnesium metal,^[1] but this procedure results in the unwanted formation of stoichiometric amounts of metal salts. One way to solve this problem is to generate the nucleophiles by C–H bond activation;^[2] however, it has been difficult to promote nucleophilic addition after the C–H activation step. Although nucleophilic addition of species generated by C–H activation has been reported using ruthenium,^[3] rhodium,^[4] palladium,^[5] and rhenium^[6] catalysts, it has been difficult to catalyze such reactions using fourth-row transition-metal complexes.^[7] We report herein that 1) complexes of manganese, a fourth-row transition metal, can be employed for C–H bond activation of aromatic compounds; 2) insertion of aldehydes into C–H bonds occurs to give benzyl alcohols; and 3) catalytic transformation is achieved with the manganese complex by the addition of Et₃SiH.

We initially investigated stoichiometric C–H bond activation and insertion of aldehydes with the manganese complex [MnBr(CO)₅]. A mixture of 1-methyl-2-phenyl-1H-imidazole (**1a**) and [MnBr(CO)₅] in toluene was heated at 100 °C for 5 min, at which point a solution of benzaldehyde (**2a**) was added. The mixture was heated at reflux for 10 h to give alcohol **3** in 52 % yield (Scheme 1). Although stoichiometric C–H bond activation and insertion of the aldehyde occurred with [MnBr(CO)₅], only a trace amount of **3** was produced with a catalytic amount of the manganese complex.



Scheme 1. Stoichiometric insertion of aldehyde into a C–H bond. TBAF = tetra-*n*-butylammonium fluoride

To recycle the manganese complex, 2.0 equiv of triethylsilane (**4**) was added to the reaction mixture from the beginning. As a result, silyl ether **5a** was obtained in 93 % yield with 5 mol % [MnBr(CO)₅].^[8,9] We examined the catalytic activity of several metal complexes using the reaction between **1a**, **2a**, and **4** as a probe. A different manganese complex, [Mn₂(CO)₁₀], showed similar catalytic activities (82 % yield of **5a**). However, the reaction did not proceed at all with the following metal complexes: [MnCl₂], [Mn(acac)₃] (acac = acetylacetonate), [(ReBr(CO)₃(thf))₂],^[6] [ReBr(CO)₅], [Ru₃(CO)₁₂], [RuH₂(CO)(PPh₃)₃], [RhCl(PPh₃)₃], and [Ir₄(CO)₁₂].^[10]

At the next stage, we investigated several aldehydes (Table 1). Aromatic aldehydes with an electron-donating or

Table 1: Reactions between **1a** and several aldehydes.^[a]

Entry	Substrate	R	Product	Yield [%] ^[b]
1	2b	<i>p</i> -(MeO)C ₆ H ₄	5b	87 (89)
2	2c	<i>p</i> -(CF ₃)C ₆ H ₄	5c	87 (89)
3	2d	<i>o</i> -MeC ₆ H ₄	5d	59 (60)
4 ^[c]	2e	<i>n</i> -C ₈ H ₁₇	5e	75 (79)
5 ^[c]	2f	<i>n</i> -C ₁₀ H ₂₁	5f	56 (57)
6 ^[d]	2g	2-furylmethyl	5g	66 (67)
7	2h	2-thienylmethyl	5h	48 (50)

[a] **2** (2.0 equiv); **4** (2.0 equiv). [b] Yield of isolated product. The yield determined by ¹H NMR spectroscopy is reported in parentheses. [c] 135 °C. [d] 48 h.

an electron-withdrawing group at the *para* position (**2b** and **2c**) gave the corresponding silyl ethers in 87 % yield (Table 1, entries 1 and 2). Using an aldehyde with a methyl group at the *ortho* position (**2d**), the yield of the silyl ether slightly decreased, probably because of the steric hindrance (Table 1, entry 3). By the reactions of alkyl aldehydes **2e** and **2f**, the corresponding silyl ethers **5e** and **5f** were formed in 75 % and

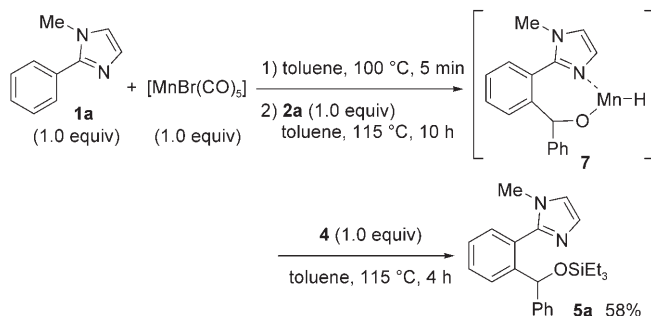
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[**] Financial support by a Grant-in-Aid for Scientific Research on Priority Areas (No. 18037049, "Advanced Molecular Transformations of Carbon Resources") from the Ministry of Education, Culture, Sports, Science, and Technology of Japan, and for Young Scientists (B) (No. 18750088) from Japan Society for the Promotion of Science, and Okayama Foundation for Science and Technology is gratefully acknowledged. We thank Dr. Teruhiko Nitoda (The MS Laboratory of Faculty of Agriculture, Okayama University) for acquiring HR-MS spectra.

Supporting information for this article is available on the WWW under <http://www.angewandte.org> or from the author.

56% yields, respectively (Table 1, entries 4 and 5). Heteroaromatic aldehydes **2g** and **2h** also provided the corresponding silyl ethers **5g** and **5h** in moderate yields (Table 1, entries 6 and 7).

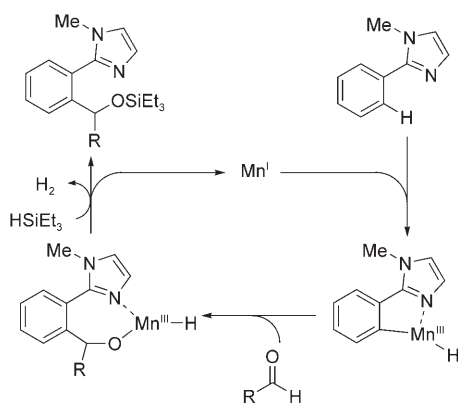
To determine the reaction mechanism, we examined the sequential transformation via intermediate **7** (Scheme 2).



Scheme 2. Manganese-mediated insertion of aldehyde into a C–H bond.

Treatment of **1a** with a stoichiometric amount of the manganese complex in toluene at 100 °C for five minutes, followed by addition of benzaldehyde (**2a**) and heating to reflux for ten hours gave the possible intermediate **7**. Then hydrosilane **4** was added to the reaction mixture and further heating resulted in the formation of silyl ether **5a** in 58% yield. This result indicates that hydrosilane **4** promotes reductive elimination of manganese by silylation of an alkoxy moiety.

The proposed mechanism is as follows (Scheme 3): 1) oxidative addition of an aromatic compound to a manga-



Scheme 3. Proposed mechanism for the formation of silyl ethers.

nese center (C–H bond activation);^[11] 2) insertion of an aldehyde into the manganese–carbon (aryl) bond. In this step, the polarity of the manganese–carbon bond is an important factor affecting the insertion of the aldehyde (a polar molecule) into the C–MnH bond; 3) silyl protection via the formation of dihydrogen.

This reaction could also be applied to asymmetric transformation.^[12] By the reaction of chiral imidazolines **8a** and **8b**

and benzaldehyde (**2a**) with triethylsilane (**4**) in the presence of manganese catalyst $[\text{MnBr}(\text{CO})_5]$, an asymmetric reaction proceeded, and a mixture of diastereomers of silyl ethers **9a** and **9b**, respectively, was obtained in moderate diastereomeric excess (Table 2, entries 1 and 2). When we used

Table 2: Asymmetric reactions of chiral imidazoline **8** with **2** and **4**.^[a]

Reaction scheme showing the synthesis of product **9** from chiral imidazoline **8**, aldehyde **2**, and triethylsilane **4** using $[\text{MnBr}(\text{CO})_5]$ (5.0 mol%) in toluene at 115°C for 24 h.

Entry	R	R'	Yield of product [%] ^[b]	de [%]
1	Ph (8a)	Ph (2a)	9a	60
2	PhCH ₂ (8b)	Ph (2a)	9b	72
3	<i>i</i> Pr (8c)	Ph (2a)	9c	80
4	<i>i</i> Pr (8c)	<i>n</i> C ₈ H ₁₇ (2e)	9d	68

[a] **2** (2.0 equiv); **4** (2.0 equiv). [b] Yield of isolated product.

imidazoline **8c** bearing an isopropyl group at the stereogenic center, the corresponding silyl ether **9c** was provided in high yield and diastereomeric excess (Table 2, entry 3). Using alkyl aldehyde **2e**, the diastereomeric excess of silyl ether **9d** decreased to 38% (Table 2, entry 4).

In summary, we have succeeded in the insertion of an aldehyde into a C–H bond of an aromatic compound using a manganese catalyst, $[\text{MnBr}(\text{CO})_5]$. In this reaction, the polarity of the manganese–carbon bond in the intermediate manganese complex is an important factor for promoting the insertion of aldehydes (polar molecules) into the C–H bond. This reaction could be applied to asymmetric transformation using an aromatic compound with a chiral substituent. Further insertion reactions, promoted by manganese complexes, of polar molecules into a C–H bond are currently being investigated.

Experimental Section

A mixture of aromatic compound **1** or **8** (0.250 mmol), aldehyde **2** (0.500 mmol), hydrosilane **4** (0.500 mmol), $[\text{MnBr}(\text{CO})_5]$ (3.4 mg, 0.0125 mmol), and toluene (1.0 mL) was stirred at 115 °C for 24 h. The product was isolated by column chromatography on silica gel, using hexane/ethyl acetate 3:1 as eluent, to give **5** or **9**.

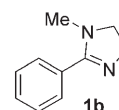
Received: May 22, 2007

Keywords: aldehydes · asymmetric synthesis · C–H activation · manganese · silyl ethers

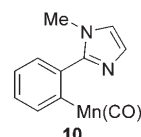
[1] For a book of Grignard reactions, see: *Grignard Reagents: New Developments* (Ed.: H. G. Richey), Wiley, New York, **2000**; *Handbook of Grignard Reagents* (Eds.: G. S. Silverman, P. E. Rakita), Marcel Dekker, New York, **1996**.

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- [7] Nucleophilic addition with fourth-row metal complexes by catalytic C–H activation is still rare. However, there are several examples of the insertion of nonpolar unsaturated molecules initiated by C–H fission with complexes of fourth-row metals, see: a) Co: G. Halbritter, F. Knoch, H. Kisch, *J. Organomet. Chem.* **1995**, 492, 87–98; b) Ni: Y. Nakao, K. S. Kanyiva, S. Oda, T. Hiyama, *J. Am. Chem. Soc.* **2006**, 128, 8146–8147.
- [8] Investigation of hydrosilanes: triethylsilane 93%; diethylmethylsilane 59%, dimethylphenylsilane 53%; triphenylsilane 77%. This reaction did not proceed using the following silanes: diphenylsilane, tris(trimethylsilyl)silane, hexamethyldisilane, hexamethyldisilazane.
- [9] 4,5-Dihydro-1-methyl-2-phenyl-1*H*-imidazole **1b** also afforded the corresponding silyl ether **6** in 72% yield.



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